

PATENT

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I hereby certify under 37 C.F.R. § 1.8(a) that this correspondence is being deposited with the United States Postal Service as **first class mail** with sufficient postage on the date indicated above and is addressed to Mail Stop AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Tracy Simmons

Printed name of person mailing correspondence

Tracy Simmons

Signature of person mailing correspondence

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Roy A. Gravel et al.	Art Unit:	1632
Serial No.:	09/487,841	Examiner:	Shin-Lin Chen
Filed:	January 19, 2000	Customer No.:	21559
Title:	HUMAN METHIONINE SYNTHASE REDUCTASE: CLONING, AND METHODS FOR EVALUATING RISK OF, PREVENTING, OR TREATING NEURAL TUBE DEFECTS, CARDIOVASCULAR DISEASE, CANCER, AND DOWN'S SYNDROME		

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STATEMENT UNDER 37 C.F.R. § 1.821

Enclosed is a Sequence Listing in accordance with the requirements of 37 C.F.R.

§§ 1.821 through 1.825 and consisting of 28 pages.

As required by 37 C.F.R. § 1.821(c), the Sequence Listing appears as a separate part of the application. Each sequence in the application appears separately in the Sequence Listing, and each sequence in the Sequence Listing is assigned a separate sequence identifier.

As required by 37 C.F.R. § 1.821(d), the sequence identifiers are used throughout

the application description and claims to refer to their respective sequences.

As required by 37 C.F.R. § 1.821(e), enclosed is a diskette containing a copy of the Sequence Listing in computer readable form.

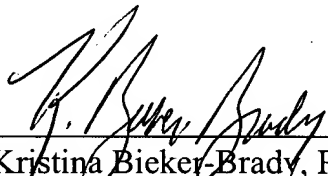
As required by 37 C.F.R. § 1.821(f), I hereby state that the contents of the computer readable form of the Sequence Listing are the same as the contents of the paper copy.

As required by 37 C.F.R. § 1.821(g), I hereby state that this submission contains no new matter.

If there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: December 15, 2004



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Reg. No. 39,109

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Boston, MA 02110
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SEQUENCE LISTING

<110> Gravel, Roy A,
Rozen, Rima
Leclerc, Daniel
Wilson, Aaron
Rosenblatt, David

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CLONING, AND METHODS FOR EVALUATING RISK OF NEURAL TUBE
DEFECTS, CARDIOVASCULAR DISEASE, CANCER, AND DOWN'S SYNDROME

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Asp	Ser	Glu	Val	Gln	Ser	Leu	Leu	Gln	Arg	Leu	Gln	Leu	Glu	Asp	Lys
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Arg	Glu	His	Cys	Val	Leu	Leu	Lys	Ile	Lys	Ala	Asp	Thr	Lys	Lys	Lys
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Gly	Ala	Thr	Leu	Pro	Gln	His	Ile	Pro	Ala	Gly	Cys	Ser	Leu	Gln	Phe

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370	Leu Arg Ala Leu Val Asp Tyr Thr Ser Asp Ser Ala Glu Lys Arg Arg	380	
385	Leu Gln Glu Leu Cys Ser Lys Gln Gly Ala Ala Asp Tyr Ser Arg Phe	395	400
405	Val Arg Asp Ala Cys Ala Cys Leu Leu Asp Leu Leu Leu Ala Phe Pro	410	415
420	Ser Cys Gln Pro Pro Leu Ser Leu Leu Glu His Leu Pro Lys Leu	425	430
435	Gln Pro Arg Pro Tyr Ser Cys Ala Ser Ser Ser Leu Phe His Pro Gly	440	445
450	Lys Leu His Phe Val Phe Asn Ile Val Glu Phe Leu Ser Thr Ala Thr	455	460
465	Thr Glu Val Leu Arg Lys Gly Val Cys Thr Gly Trp Leu Ala Leu Leu	470	475
485	Val Ala Ser Val Leu Gln Pro Asn Ile His Ala Ser His Glu Asp Ser	490	495
500	Gly Lys Ala Leu Ala Pro Lys Ile Ser Ile Ser Pro Arg Thr Thr Asn	505	510
515	Ser Phe His Leu Pro Asp Asp Pro Ser Ile Pro Ile Ile Met Val Gly	520	525
530	Pro Gly Thr Gly Ile Ala Pro Phe Ile Gly Phe Leu Gln His Arg Glu	535	540
545	Lys Leu Gln Glu Gln His Pro Asp Gly Asn Phe Gly Ala Met Trp Leu	550	555
565	Phe Phe Gly Cys Arg His Lys Asp Arg Asp Tyr Leu Phe Arg Lys Glu	570	575
580	Leu Arg His Phe Leu Lys His Gly Ile Leu Thr His Leu Lys Val Ser	585	590
595	Phe Ser Arg Asp Ala Pro Val Gly Glu Glu Glu Ala Pro Ala Lys Tyr	600	605
610	Val Gln Asp Asn Ile Gln Leu His Gly Gln Gln Val Ala Arg Ile Leu	615	620
625	Leu Gln Glu Asn Gly His Ile Tyr Val Cys Gly Asp Ala Lys Asn Met	630	635
645	Ala Lys Asp Val His Asp Ala Leu Val Gln Ile Ile Ser Lys Glu Val	650	655
660	Gly Val Glu Lys Leu Glu Ala Met Lys Thr Leu Ala Thr Leu Lys Glu	665	670
675	Glu Lys Arg Tyr Leu Gln Asp Ile Trp Ser	680	685
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<211> 2094

<212> DNA

<213> Homo sapiens

<400> 45

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<210> 46

<211> 697

<212> PRT

<213> Homo sapiens

<400> 46

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Ala Asp Leu His Cys Ile Ser Glu Ser Asp Lys Tyr Asp Leu Lys Thr
          35          40          45
Glu Thr Ala Pro Leu Val Val Val Ser Thr Thr Gly Thr Gly Asp
          50          55          60
Pro Pro Asp Thr Ala Arg Lys Phe Val Lys Glu Ile Gln Asn Gln Thr
65          70          75          80
Leu Pro Val Asp Phe Phe Ala His Leu Arg Tyr Gly Leu Leu Gly Leu
          85          90          95
Gly Asp Ser Glu Tyr Thr Tyr Phe Cys Asn Gly Gly Lys Ile Ile Asp
          100         105         110
Lys Arg Leu Gln Glu Leu Gly Ala Arg His Phe Tyr Asp Thr Gly His
          115         120         125
Ala Asp Asp Cys Val Gly Leu Glu Leu Val Val Glu Pro Trp Ile Ala
          130         135         140
Gly Leu Trp Pro Ala Leu Arg Lys His Phe Arg Ser Ser Arg Gly Gln
145         150         155         160
Glu Glu Ile Ser Gly Ala Leu Pro Val Ala Ser Pro Ala Ser Leu Arg

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Gln	Asn	Ala	Val	Asn	Ser	Asn	Gln	Ser	Asn	Val	Val	Ile	Glu	Asp	Phe
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				245					250					255	
Ser	Leu	Gly	Gln	Glu	Glu	Ser	Gln	Val	Ser	Val	Thr	Ser	Ala	Asp	Pro
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Ile	Phe	Thr	Trp	Cys	Leu	Glu	Ile	Arg	Ala	Ile	Pro	Lys	Lys	Ala	Phe
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Leu	Arg	Ala	Leu	Val	Asp	Tyr	Thr	Ser	Asp	Ser	Ala	Glu	Lys	Arg	Arg
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Leu	Gln	Glu	Leu	Cys	Ser	Lys	Gln	Gly	Ala	Ala	Asp	Tyr	Ser	Arg	Phe
				405					410					415	
Val	Arg	Asp	Ala	Cys	Ala	Cys	Leu	Leu	Asp	Leu	Leu	Leu	Ala	Phe	Pro
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Ser	Cys	Gln	Pro	Pro	Leu	Ser	Leu	Leu	Leu	Glu	His	Leu	Pro	Lys	Leu
		435					440					445			
Gln	Pro	Arg	Pro	Tyr	Ser	Cys	Ala	Ser	Ser	Ser	Leu	Phe	His	Pro	Gly
	450					455					460				
Lys	Leu	His	Phe	Val	Phe	Asn	Ile	Val	Glu	Phe	Leu	Ser	Thr	Ala	Thr
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Thr	Glu	Val	Leu	Arg	Lys	Gly	Val	Cys	Thr	Gly	Trp	Leu	Ala	Leu	Leu
				485					490					495	
Val	Ala	Ser	Val	Leu	Gln	Pro	Asn	Ile	His	Ala	Ser	His	Glu	Asp	Ser
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Gln	Asp	Asn	Ile	Gln	Leu	His	Gly	Gln	Gln	Val	Ala	Arg	Ile	Leu	Leu
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Gln	Glu	Asn	Gly	His	Ile	Tyr	Val	Cys	Gly	Asp	Ala	Lys	Asn	Met	Ala
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Lys	Asp	Val	His	Asp	Ala	Leu	Val	Gln	Ile	Ile	Ser	Lys	Glu	Val	Gly
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Val	Glu	Lys	Leu	Glu	Ala	Met	Lys	Thr	Leu	Ala	Thr	Leu	Lys	Glu	Glu
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 <212> DNA
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 <211> 689
 <212> PRT

<213> Homo sapiens

<400> 48

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Pro	Asp	Thr	Ala	Arg	Lys	Phe	Val	Lys	Glu	Ile	Gln	Asn	Gln	Thr	Leu
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Pro	Val	Asp	Phe	Phe	Ala	His	Leu	Arg	Tyr	Gly	Leu	Leu	Gly	Leu	Gly
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Gln	Glu	Leu	Cys	Ser	Lys	Gln	Gly	Ala	Ala	Asp	Tyr	Ser	Arg	Phe	Val
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Arg	Asp	Ala	Cys	Ala	Cys	Leu	Leu	Asp	Leu	Leu	Leu	Ala	Phe	Pro	Ser
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 Leu His Phe Val Phe Asn Ile Val Glu Phe Leu Ser Thr Ala Thr Thr
 465 470 475 480
 Glu Val Leu Arg Lys Gly Val Cys Thr Gly Trp Leu Ala Leu Leu Val
 485 490 495
 Ala Ser Val Leu Gln Pro Asn Ile His Ala Ser His Glu Asp Ser Gly
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 Lys Ala Leu Ala Pro Lys Ile Ser Ile Ser Pro Arg Thr Thr Asn Ser
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 645 650 655
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